REMARKS

Claims 1- 42 are being examined on their merits. Claims 43-66 stand withdrawn from consideration pursuant to a restriction requirement under 35 U.S.C. § 121.

Priority

Applicants request withdrawal of the rejection without prejudice or disclaimer in light of their amendment to page 1 of the specification.

Information Disclosure Statements

Applicants thank the Examiner for returning signed copies of pages 1, 2 and 4 of the Information Disclosure Statement filed September 24, 2002. Applicants, note that they did not received a signed and initialed copy of page 3 of the information disclosure statement, and request the Examiner forward a signed and initialed copy of page 3 with the next communication.

Figures

Applicants thank the Examiner for the indication that the previously filed drawings are acceptable.

Rejection under 35 U.S.C. § 112

Claims 1, 2, 4-8, 10-16, 18-24, 26-34, 36-39, 41, and 42 stand rejected under 112 second paragraph as allegedly being indefinite for the recitation of a "batimastat compound." In the Office Action, the Examiner contends that "no definition of what constitutes 'a batimastat compound' is found in the claim or the body of the specification." Applicants respectfully point out that the claims are to be read in light of the specification. *See in re Vogel*, 422 F.2d 438, 441, 164 U.S.P.Q. 619, 622 (C.C.P.A. 1970). The test for determining whether terms in a given claim are indefinite is

whether one skilled in the art would understand what is claimed. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991). A person of ordinary skill in the art would understand the metes and bounds of the claims when read in light of the specification, which clearly and distinctly sets forth the meaning of a "batimastat compound" at page 8, especially lines 10 through 16 and the associated figure. As such, reconsideration and withdrawal of this rejection are respectfully requested.

Rejection under 35 U.S.C. 103

Claims 1-42 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over US 5,767,153 and WO 97/41844 or US 5,763,621.

In the Office Action dated February 26, 2003 the Examiner alleges that it would have been *prima facie* obvious to substitute the batimastat compositions taught in the '153 patent by Bowman *et al.* for the batimastat compositions taught by either the WO 97/41844 publication (herein after '41844) or the '621 patent.

Applicants respectfully disagree and submit that the Examiner has failed to establish a *prima facie* case of obviousness. The Examiner bears the initial burden of establishing a *prima facie* case of obviousness § 103, *In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988), in which at least the following two criteria must be met: 1) there must be some suggestion or motivation to modify or combine references and 2) there must be a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). Both the suggestion or motivation to make the claimed combination, and the reasonable expectation of success, must both be found in the prior art, and not based on the applicant's disclosure. *Id.*

Applicants respectfully assert that the Examiner has not established a *prima facie* case of

obviousness because no adequate explanation of the suggestion or motivation to combine the teachings of the cited references has been provided. The arguments submitted in previous Office Actions use improper hindsight reconstruction in the formulation of the rejections. The Examiner alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to "use compositions of batimastat and polycarbophil to treat retinal neovascularization in order to obtain the results suggested by the references with a reasonable expectation of success." Office Action dated February 26, 2003 at page 4. Applicants respectfully disagree.

Applicants submit that the references, and the Examiner's argument, at the most suggest that it might be "obvious-to-try" the claimed methods of treatment, but that the cited references do not establish a reasonable expectation of success in combining the teachings of the cited references. One of skill in the art would have no reasonable expectation that topical administration to the eye would be an effective means to accomplish delivery of a therapeutic to the retina, which is located in the posterior segment of the eye on the contralateral side of the sclera. [1] Indeed, while the art recognized that recent advances had been made in topical drug delivery to the eye, "delivery of therapeutic doses of drugs to the tissue in the posterior segment of the eye, however, remains a significant challenge." *See n. 1*, at 461. This art-recognized difficulty is not addressed by the cited references.

Moreover, in making the allegation of obviousness a prior art reference must be considered in its entirety, including portions that would lead away from the invention. *W.L. Gore v. Garlock*, 721, F.2d 1540, 220 U.S.P.Q. 303 (Fed. Cir. 1983). The Examiner, in making the allegation of obviousness has not only failed to identify specific portions of the cited disclosures allegedly

1 Dayle H. Geroski and Henry F. Edlehauser, *Drug Delivery for Posterior Segment EyeDisease,* ARVO 41(5) 961-4 (2000).

teaching the use of topical formulations for the treatment of retinal disorders, but has also virtually ignored the portions of the disclosures that teach away from the invention.

More specifically, with regard to the '41844 publication, Applicants submit that the reference only teaches topical formulations suitable for "preventing glaucoma filtration bleb failure or scar formation associated with ophthalmic surgery," and that the reference discloses topical dosage forms for treatment of "pterygium, hyperkeratosis, and cheloid and polyp formation." See page 24 of the '41844 disclosure. Each of these disclosed uses are for the treatment of tissues directly accessible to the topical formulation, and none of the disclosed uses require delivery of a batimastat compound to the posterior segment of the eye and across the scleral tissue to the retina. In this regard, Applicants submit that the '41844 disclosure would at most suggest to the skilled artisan that topical batimastat application was effective to treat accessible tissues.

The Examiner has similarly failed to identify portions of the '621 disclosure that teach the use of topical ophthalmic formulations for the delivery of a batimastat compound, or for that matter any matrix metalloproteinase inhibitor, to the retinal tissue. To the extent that the '621 patent might discuss topical administration to the eye, the disclosure dose not address topical administration of batimastat or its bioavailibility to the retina. The only passage of the '621 patent that discusses batimastat (BB94, column 3, lines 36-47) acknowledges its poor bioavailability upon **oral** administration, and asserts the superior **oral** bioavailability of other disclosed matrix metalloproteinase inhibitors. Such a statement neither suggests the claimed methods of treating retinal neovascularization by topically administered batimastat, nor provides any reasonable expectation of success with regard to the use of batimastat as discussed below. Applicants respectfully submit that in view of the foregoing, the '621 disclosure, either alone or in combination with the '153 patent, is

insufficient to render obvious the use of topically administered batimastat for the treatment of retinal disorders. Moreover, by teaching the use of other compounds with characteristics allegedly superior to batimastat, the '621 disclosure teaches away from the claimed method of treatment employing batimastat compounds.

Applicants submit that the Examiner has only cursorily asserted the existence of a motivation to combine the references and a reasonable expectation of success, without identifying the basis for any such expectation, in either the references cited or in the art. Moreover, the Examiner has failed to consider the art-recognized difficulty in achieving therapeutically effective doses of drugs in the posterior segment of the eye with topical administration. In view of the foregoing, Applicants submit neither a motivation nor a suggestion to combine the references existed in the art, and that a prima facie case of obviousness has not been established. Accordingly, Applicants respectfully request withdrawal of the rejection.

CONCLUSION

In view of the foregoing Applicants believe the application is in condition for allowance and solicit a Notice of Allowance indicating such at the earliest possible time. The Examiner is encouraged to contact the undersigned should any additional information be necessary.

Respectfully submitted,

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